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09/933,559	08/20/2001	Veerappa S. Subramanian	4961-5	6556

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EXAMINER	
YOUNG, MICAH PAUL	
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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/933,559
Filing Date: August 20, 2001
Appellant(s): SUBRAMANIAN ET AL.

Kent H Cheng
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 3/11/05.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 1-17 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

4,680,323	LOWEY	7-1987
4,687,660	BAKER et al	8-1987
6,033,686	SETH	3-2000

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-17 are rejected under 35 U.S.C. 103(a). This rejection is set forth in a prior Office Action, mailed on 6/15/2004.

(11) Response to Argument

Applicant argues that a *prima facie* obviousness case has not been established. Applicant argues that the '323 Patent does not teach carboxyvinyl polymers as sole control releasing agents; the '660 patent does not remedy this deficiency and neither does the '686 patent. Applicant also argues that there is no motivation for combining these references. Applicant further argues that even if combined these references would result in a different formulation that that of the instant claims. The Examiner has requested an evidence showing the criticality of the present invention yet applicant argues that since no *prima facie* case has been established, according to Applicant, this evidence has not been presented. Applicant also argues that the microcrystalline cellulose and lactose used in the instant case are not rate controlling agents as asserted by the Examiner.

In response the Examiner respectfully disagrees with each and every aspect of Applicants' arguments. It is the position of the Examiner that the combination of the prior art ('323, '660 and '686 patents) obviate the instant claims.

First, the Examiner again draws Applicant's attention to page 4, paragraph 2 of the presently presented Specification. Here Applicant states:

> "The present invention also provides for a pharmaceutical composition designed for sustained (SR) tablets, containing bupropion hydrochloride and carboxyvinyl polymer (Carbopol) and other pharmaceutically acceptable excipients, **preferably lactose and microcrystalline cellulose for controlling the rate of release of the active ingredient** for twice a day and once a day dosage regimen."

It is here that the Examiner bases his argument. Applicant claims that carboxyvinyl polymer is the sole stabilizing and rate controlling polymer, yet recognizes in the specification that lactose and microcrystalline cellulose are used for controlling the rate of release. Applicant also argued that this was not the intent of the passage, yet the Examiner must give each passage and each claims their broadest reasonable interpretation. Applicant has argued that lactose and microcrystalline cellulose are not rate controller but are merely diluents and disintegrants. However, as recognized by Remington's Pharmaceutical Sciences, vol. II, disintegrants facilitate a tablet's "breakup or disintegration after administration." (pg. 1617) These substances effect how fast or slowly an active agent is absorbed into the body, thereby controlling the rate of release of the active substance. Whether releasing quickly or slowly, a disintegrants will affect the rate of release of the active agent to a patient. With this view in mind the Examiner reminds Applicant that a substance and its properties are inseparable. Remington's further teaches that substances usually carry more than once function in final formulations, such as hydroxypropylcellulose being "used both as an aid to prolong the release of from the tablet, as

well as a film former in the tablet." (pg. 1617) Whether intended or not the inclusion of lactose and microcrystalline cellulose would impart their particular rate controlling properties into the final formulation.

With these aspects in mind, the Examiner draws Applicant's attention to the prior art of record. As discussed in the prior Office Actions of record, the '323 reference teaches a long acting controlled release formulation comprising carboxyvinyl polymer (Carbopol), usually in concentrations between 1-20%, as well as excipients (Examples). The tablet releases its active agents over a 24-hour period (col. 3, lin 55-60). The reference lists sedatives, and tranquilizers as possible active ingredients (col. 6, lin. 6-9). The '323 reference though suggestive of sedatives and tranquilizers is silent to the inclusion of bupropion. However as seen in the '660 and '686 patents, the combination of bupropion hydrochloride with rate controlling polymers is well within the level of skill in the art. The '660 patent discloses bupropion hydrochloride in combination with water soluble polymers such as lactose, as well as insoluble polymers such as cellulose acetates and ethyl cellulose (examples). The '686 patent discloses a sustained release formulation of bupropion hydrochloride along with rate controlling polymers and excipients including microcrystalline cellulose, and lactose col. 2, lin. 13-16). The formulation releases bupropion hydrochloride at a rate of, 30-60% after 1 hour, 55-80% after 2 hours, 75-95% after 3 hours, and 80-100% after 4 hours (col. 3, lin 40-56). This is compared to 30-45% in hour 60-80% in 4 hours and not less than 85% in 7 hours for the instant claims. It can be seen that this release profile is well within the level of skill in the art. Also disclosed in reference, a method for formulating the composition comprising mixing the constituents and granulating them with purified water (examples).

With these aspects in mind a skilled artisan would have been motivated to combine the bupropion HCL of '660 into the formulation of '323 in order to impart stability and proper release of the agent. A skilled artisan would have been able to make the substitution since both references share excipients, active agents, and operate within the same field of endeavor. A skilled artisan would have been able to substitute the bupropion HCL of '660 into the formulation of '323, along with the lactose of the formulation in order the effect the release of the drug. Release profiles can be manipulated through concentrations of the non-active excipients, and is within the level of skill in the art. A skilled artisan would have further been motivated to combine the purified water and further excipients of '680 in order to better refine the processing and release profile of the active agent. '680 releases bupropion HCL with ethyl cellulose as a possible excipient, similar to '660. A skilled artisan would have been motivated to make these combinations and substitutions in order to optimize the release of a bupropion HCL tablet. An expected result of such a combination would have been a tablet with a release profile and consistency useful as an anti-depressant.

Regarding Applicant's argument that a different product would result from this combination where carboxyvinyl polymer is not the sole rate controller and that the formulation would further include hydroxypropylmethylcellulose, and hydroxypropyl cellulose, the Examiner reminds Applicant that first the language of the claims is open and thereby can include many substances as long as they are not detrimental to the overall function of the resulting formulation; secondly as discussed in Remington's, substances can and do often have multiple functions when placed into tablets. The cellulosic polymers present in the combination postulated by Applicant

could act as both rate controllers, film-forming agents, binders and fillers, as is the nature of cellulosic polymers.

It is the position of the Examiner that '323 provided sufficient motivation to include the active agents and excipients of both '660 and '680. It is further the position of the Examiner that the release profiles recited in the instant claims would be well within in the level of skill in the art to reproduce as a result of routine experimentation. It is lastly the position of the Examiner that the proposed combination of prior art provides a *prima facie* case of obviousness that Applicant has yet to overcome. The burden of proof that was shifted to applicant has not been met in establishing the patentable distinction between the formulation of the instant claims and that of the prior art. For these reasons the claims remain obviated by the combination of '323, '660 and '668.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Examiner
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May 31, 2005

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